

REMARKS/ARGUMENTS

As an initial matter, Applicant wishes to thank Examiner Kishore for the courtesies extended to Applicant's representatives in the interview on April 9, 2008, and the follow-up discussions. During these discussions, Applicant's representatives pointed out the differences between the pending claims and the cited art, in particular, the differences between the liposomes disclosed by Hristova and the currently claimed invention.

By this Supplemental Amendment, claims 176 and 183 are amended. No new matter has been added. Applicant intends to pursue the subject matter of the canceled claims in one or more continuation and/or divisional applications. Claims 176-189 are currently pending the present application.

Applicant respectfully requests entry of the After-Final Amendment filed February 25, 2008 and the present Supplemental Amendment, and consideration of the claims in view of the following remarks.

Rejection of claims 66, 69, 77, 93, 97, 116-118, 121-122, 124-125, 128, 131-136, and 162-169 under 35 USC §102(b) as anticipated by Eibl US Patent No. 5, 626,867

The Examiner has rejected claims 66, 69, 77, 93, 97, 116-118, 121-122, 124-125, 128, 131-136, and 162-169 under 35 USC § 102(b) as anticipated by Eibl US Patent No. 5, 626,867.

As previously noted, Applicant has canceled these claims without prejudice or disclaimer in the After-Final Amendment filed February 25, 2008, which was entered with the Request for Continued Examination filed March 25, 2008. Accordingly, this rejection is moot. Applicant intends to pursue these claims in one or more divisional and/or continuation applications.

Rejection of claims 66-71, 73, 74, 76-83, 93, 97-103, 116-156, and 176-189 under 35 U.S.C. § 103(a) as obvious over Hristova, et al. Micromolecules, vol. 28, pp. 7693-7699, 1995 in combination with Ogawa et al. US Patent No. 5,094,854.

The Examiner has rejected claims 66-71, 73, 74, 76-83, 93, 97-103, 116-156, and 176-189 under 35 U.S.C. § 103(a) as obvious over Hristova, et al. Micromolecules, vol. 28, pp. 7693-7699, 1995 (hereinafter "Hristova") in combination with Ogawa et al. US Patent No. 5,094,854 (hereinafter "Ogawa"). Applicant respectfully requests reconsideration and withdrawal of this rejection.

As previously noted, the rejection of claims 66-71, 73, 74, 76-83, 93, 97-103, and 116-156 is rendered moot, in view of the After-Final Amendment filed February 25, 2008, which was entered with the RCE filed March 25, 2008. The following remarks will consider this rejection as applied to claims 176-189.

As shown above, independent claims 176 and 183 have been amended to recite an active agent selected from the group consisting of a pharmacologically active agent, a therapeutic agent, a diagnostic or imaging agent, and combinations thereof. Independent claim 176, and claims 177-182 dependent thereon, require, *inter alia*, a liposome having a gel-phase bilayer membrane, comprising:

- (a) a first component which is dipalmitoylphosphatidylcholine (DPPC) in an amount ranging from 80 to 98 mol %; and
- (b) a second component selected from the group consisting of: (i) monostearoylphosphatidylcholine (MSPC) and 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[poly(ethyleneglycol) 2000] (DSPE-PEG-2000) in an amount ranging from 2 to 20 mol%; and (ii) monopalmitoylphosphatidylcholine (MPPC) and 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[poly(ethyleneglycol) 2000] (DSPE-PEG-2000) in an amount ranging from 2 to 20 mol%.

Independent claim 183, and claims 184-189 dependent thereon, require *inter alia* a liposome having a gel-phase bilayer membrane, comprising:

- (a) a first component which is dipalmitoylphosphatidylcholine (DPPC) in an amount ranging from 80 to 98 mol %; and
- (b) a second component selected from the group consisting of: (i) monostearoylphosphatidylcholine (MSPC) and 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[poly(ethyleneglycol) 2000] (DSPE-PEG-2000) in an amount ranging from 2 to 20 mol%; and (ii) monopalmitoylphosphatidylcholine (MPPC) and 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[poly(ethyleneglycol) 2000] (DSPE-PEG-2000) in an amount ranging from 2 to 20 mol%.

The Examiner asserts in the Advisory Action dated March 14, 2008, at page 2, that

although the combination taught by Hristova includes egg phosphatidylcholine, the motivation to use a saturated phospholipid such as DSPC or DPPC could derived not only from the discussion by Hristova of the gel and liquid crystalline [bilayers], but also from Ogawa who teaches the use of phospholipids with higher transition temperatures for hyperthermia.

The currently pending claims all recite specific components in specific ratios. Neither the recited components nor the ratios are disclosed in the cited art. Neither Hristova nor Ogawa describe the second component of present claims 176 and 183, or any such combination whatsoever.

In particular, there is no description or suggestion of a second component selected from any of the following or combinations thereof:

monostearoylphosphatidylcholine (MSPC),
1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[poly(ethyleneglycol) 2000]
(DSPE-PEG-2000), and
monopalmitoylphosphatidylcholine (MPPC),
or their recited amounts.

As such, even assuming *argumendo* that DSPC or DPPC could be derived from the references for a liposome bilayer, there is still no indication of the use or suggestion of a combination that includes the claimed second component in a gel-phase bilayer.

Regarding Ogawa, Applicant notes that the reference selectively describes several possible liposome compositions, including a combination of DPPC and MPPC. *See* column 2, lines 59-61. However, the MPPC described in the reference is entirely different from the present claims. In particular, the MPPC in the reference represents myristoylpalmitoylphosphatidyl choline, while the present claims recite monopalmitoylphosphatidyl choline as the MPPC. Ogawa does not teach or suggest the currently claimed second components.

The deficiencies of Ogawa are not cured by Hristova. Applicant points out that the liposome described in the reference is *structurally* different from the present claims. In

particular, as previously noted, Hristova describes a liposome comprising POPE-PEG:EPC:MOPC, in which EPC (egg phosphatidylcholine) forms a liquid crystalline bilayer, not a gel-phase bilayer as required in the structure of the claimed liposome. See page 7697 (right column, last paragraph).

In the paragraph bridging pages 7697-8, Hristova describes phospholipid:lysolipid bilayers. The only lysolipid used by Hristova is MOPC (monooleoylphosphatidylcholine). Thus, Hristova does not teach or suggest the compounds that make up the currently claimed second components. Further, the ratio of lysolipid to phospholipid used by Hristova is a 1:1 mole ratio. On page 7697, right column, Hristova states “[f]or all these samples the ratio between the number of phospholipids (POPE-PEG or EPC) and lysolipid (MOPC) was 1:1.” Thus, Hristova does not teach or suggest the presently claimed ratios.

Neither cited reference alone, nor the cited references taken in combination, teach or suggest the presently claimed second components. In addition, neither reference alone, nor the references in combination teach the presently claimed ratios of first and second components. Accordingly, the claimed invention is not obvious over the references alone or in combination. Applicant respectfully requests reconsideration and withdrawal of this rejection.

Double Patenting Rejection

Claims 66-71, 73, 74, 76-83, 93, 97-103, 116-156 and 159-169, 176-189 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-68 of U.S. Patent No. 6,726,925.

As noted in the After-Final Amendment filed February 26, 2008, Applicant will submit a terminal disclaimer to obviate this rejection when the Examiner indicates the claims are allowable.

Conclusion

In view of the above amendments and remarks, Applicant believes the pending application is in condition for allowance. An expedited notification of allowance is kindly requested. If, however, there are any issues that the Examiner would like to further discuss, the Examiner is invited to contact Applicant's representative at the number listed below.

Applicant believe no fee is due with this response. However, the Commissioner is hereby authorized in this, concurrent, and further replies, to charge payment or credit any overpayment to Deposit Account No. 22-0185, under Order No. 14514-00007-US1 from which the undersigned is authorized to draw.

Dated: April 15, 2008

Respectfully submitted,

Electronic signature: /Bryant L. Young/
Bryant L. Young
Registration No.: 49,073
CONNOLLY BOVE LODGE & HUTZ LLP
1875 Eye Street, NW
Suite 1100
Washington, DC 20006
(202) 331-7111
(202) 293-6229 (Fax)
Attorney for Applicant